REMARKS: CLAIM REJECTION UNDER 35 U.S.C. § 103(a)

In the Office Action mailed June 14, 2007 from the United States Patent and Trademark Office, the Examiner rejected claims 1 and 3-8 under 35 U.S.C. 112, First Paragraph, as failing to comply with the written description requirement. The Examiner also rejected claims 9, 10, 12 and 13 under 35 U.S.C. § 103(a) as being unpatentable over Gidlund U.S. Patent No. 6,436,449 ("Gidlund"). Accordingly, Applicant respectfully submits the following.

Rejections Under 35 U.S.C. §112

Applicant has amended the independent claims of the present application, deleting the limitation for "less than 0.1 ml per kg of body weight of a patient." Accordingly, Applicant requests that the pending Section 112 rejections be withdrawn at this time.

Rejections Under 35 U.S.C. §103

Applicant respectfully submits that Gidlund fails to teach the claim limitations recited in the present application, and no reasonable expectation for success could be based on Gidlund's limited disclosure because Gidlund teaches a method for treating tinnitus not method for treating pain through **selective** COX-2 inhibition.

Gidlund does not teach a method for reducing pain by selective COX-2 inhibition, and accordingly fails to teach every claimed limitation of the present invention. Rather, Gidlund teaches use of an extract derived from the fruits, leaves, the bark or the roots of *Morinda*

citrifolia for the manufacture of a medicament for the treatment of a mammal suffering from tinnitus. Tinnitus "is the perception of sound when no external sound is present." Gidlund, col. 2 lns55-58. Tinnitus is not pain/inflammation. Further, Gidlund fails to disclose administration of an appropriate concentration of extract to achieve selective COX-2 inhibition. Gidlund discloses that the "liquid extract from *Morinda citrifolia* will be present in an amount such as to provide a daily dosage of 0.1-2 ml, or 0.2-1 ml . . . per kg body weight of the patient" (See col. 5, ln. 15-19), with no reference to, or limitation on a concentration of the *Morinda citrifolia*-derived liquid extract whatsoever (administering between 8 and 106 ml of liquid Morinda citrifolia juice to a 80kg patient daily).

As described in example 1 of the specification of the present application, the dosaging of *citrifolia* juice is critical to achieving selective COX-2 inhibition. If an excessive amount of juice is administered, the selective COX-2 properties of the *citrifolia* juice are diminished. In particular, page 15 of the specification indicates that,

> Biochemical Assays show that a concentration of 2.31% produced an inhibition of COX- 2 which was 20%, while the inhibition of COX-1 was 10%, while the inhibition of COX- 2 was 60%. This is compared with the administration of 11% solution of *Morinda citrifolia* juice which produced an 83% inhibition of COX-1 and an 84% inhibition of COX-2. Accordingly, at greater concentrations, the selective COX-2 inhibition produced by the consumption of *Morinda citrifolia* products is limited.

Accordingly, COX-2 selective inhibition with *Morinda citrifolia* juice is sensitive to the concentration administered. Modifying the concentration of *Morinda citrifolia* juice reduces the selective COX-2 inhibition properties of the administration. Accordingly, the broad range of dosaging disclosed by Gidlund would fail to effectively produce selective COX-2 inhibition.

The difference between treatment of pain and selective COX-2 inhibition is patentable. COX-2 expression is associated with pain and inflammation. COX-1 is a constitutively active

enzyme responsible for maintaining the mucosal living of the stomach. When COX-2 is inhibited, pain is reduced. When COX-1 is inhibited, patients experience uncomfortable side effects, including gastric ulcers.

Compounds or formulations, which favorably influencing pain, do not have a reasonable probability for reducing pain by selective COX-2 inhibition. For example, a popular treatment of chronic pain and inflammation involves the use of non-steroidal anti-inflammatory drugs (NSAIDs). NSAIDs inhibit both COX-2 and COX-1.While NSAIDs have been effective in reducing inflammation and pain, NSAIDs have a number of adverse side effects. The major side effects of NSAIDs are gastrointestinal related. In order to provide relief pain associated with COX-2 without inhibiting COX-1, drug companies have attempted to produce selective COX-2 inhibitors (e.g., VIOXX).

Applicant's claims contain limitations which require that the juice be administered in a very specific amount by volume in order to limit undesired COX-1 inhibition. Applicants' disclosure demonstrates the importance and non-obviousness of administering the appropriate concentration of *Morinda citrifolia.* In particular, Applicants' experiments provide the non-obvious discovery that at some concentrations, selective COX-2 inhibition was achieved, and at other concentrations it was not. Specification, pg. 15. The Applicants indicated, "[t]he data suggests the surprising result that in some circumstances 'less' *Morinda citrifolia* juice provides 'more' inhibition selectivity." Specification, pg. 15. Applicants' disclosure shows that COX-2 selectivity is undermined by excessive, increased concentrations. Specification, pg. 15. It is only after the inherent COX-1 inhibiting qualities of *Morinda citrifolia* are limited by the methods of the present invention that selective COX-2 inhibition occurs.

Because the cited prior art fails to teach or suggest all claim limitations of the present

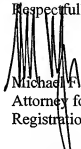
invention, Applicants submit that the present invention is not obvious.

CONCLUSION

Applicants submit that the claims are now in condition for allowance. Accordingly, Applicants request favorable reconsideration. If the Examiner has any questions or concerns regarding this communication, the Examiner is invited to call the undersigned.

DATED this 14 day of September, 2007

Respectfully submitted,



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